Declining Ovarian Cancer Rates in U.S. Women in Relation to Parity and Oral Contraceptive Use

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Ovarian cancer incidence and mortality rates have declined among U.S. women age 35–59 years during the period 1970–1995. Epidemiologic studies have shown that ovarian cancer risk decreases with increasing parity and increasing duration of oral contraceptive use. During this period, parity has declined while oral contraceptive use has increased. We compared temporal trends in observed ovarian cancer incidence rates with rates predicted by changes in parity and duration of oral contraceptive use to determine whether the changes in these characteristics could explain the declining rates in younger women. In addition, we wished to examine whether oral contraceptive use continues to be protective to postmenopausal women. To predict changes in rates between 1970 and 1995, we assumed that increases in parity and duration of oral contraceptive use induce proportional decreases in incidence rates. We found that the rates predicted by these assumptions agreed well with observed rates in young women (age 30–49) but were substantially lower than observed rates in older women (age 50–64). The data indicate that the relative decrease in incidence rates due to the protective effect of oral contraceptive use declines with age. (Epidemiology 2000;11:102–105)

Keywords: oral contraceptive use, ovarian neoplasms, parity, time trends, menopause.

In the U.S., approximately 25,200 women are diagnosed with ovarian cancer each year.[1] Some 75% of these women have advanced disease at the time of diagnosis,[1] and 5-year relative survival rates decrease sharply with increasing stage of disease at diagnosis.[1] Thus, ovarian cancer is the fifth leading cause of cancer death in U.S. women and will account for an estimated 14,500 deaths in 1999, more than half of all deaths from gynecologic cancers.[1]

Ovarian cancer incidence and mortality rates have declined during the period 1970–1995 among U.S. women age 35–59.[2–4] There is general agreement that risk decreases with greater number of pregnancies (regardless of gestational length or outcome) and greater duration of oral contraceptive (OC) use.[5] Nevertheless, although studies show that OC use is protective, the long-term effects of premenopausal use on ovarian cancer risk in postmenopausal women are not clear, because OCs were introduced in the 1960s, and thus the earliest cohorts of users are only now reaching their sixth and seventh decades. Here, we examined whether temporal changes in parity and OC use could account for the observed declines in cancer incidence rates, particularly in postmenopausal women age 50–64.

Subjects and Methods

We calculated incidence rates of ovarian cancer of all histologies, in women of all ethnic groups, using data from five geographic areas (Atlanta, Detroit, San Francisco, Connecticut, and Iowa) obtained from the Third National Cancer Survey and from the Surveillance, Epidemiology, and End Results Program of the U.S. National Cancer Institute.[2,3] Incidence rates were calculated for the periods 1969–1971, 1973–1977, 1978–1982, 1983–1987, 1988–1992, and 1995. Data for women with tumors of low malignant potential were not recorded throughout all of these periods, and so these women have been excluded from all rates.

Ovarian cancer mortality rates are based on counts from the U.S. National Center for Health Statistics (NCHS) and on population estimates from the U.S. census. Rates are calculated for the periods 1968–1972, 1973–1977, 1978–1982, 1983–1987, 1989–1991, and 1994–1996. Incidence and mortality rates for 5-year age groups, expressed as number of cancers (or deaths) per 100,000 woman-years, were calculated using as denom-

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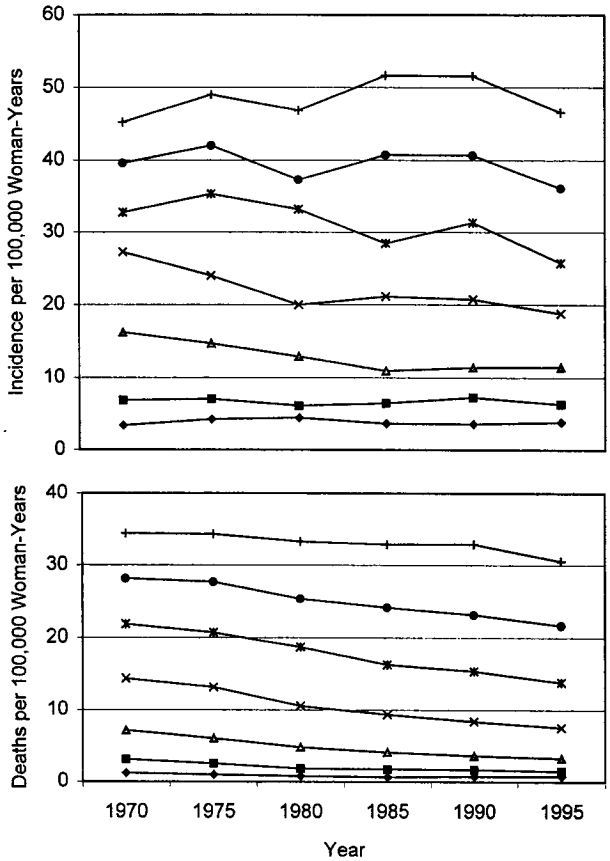

FIGURE 1. Observed ovarian cancer rates, 1970–1995. Ages (years): ♦ = 30–34; ▩ = 35–39; △ = 40–44; × = 45–49; ✻ = 50–54; ● = 55–59; + = 60–64.

inators estimated counts of women with at least one intact ovary, with data provided by Brett *et al.*[4]

We used NCHS data[6] to obtain the average number of childbirths in women age 30–34, 35–39, 40–44, 45–49, and 50–54 in the calendar years 1950, 1955, 1960, 1965, 1970, 1975, 1980, 1985, 1990, and 1994, the most recent year for which data are available. For those women age 30–54 in 1995, we used 1994 data, on the basis of the assumption that these data are a good approximation for women in 1995. Rates are based on births adjusted for underregistration and on number of women adjusted for underenumeration and misstatements of age in censuses.

The age-specific durations of OC use among women age 30–34, 35–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, and 70–74 in 1995 were calculated by multiplying the prevalence of ever-use of OCs (*OC prevalence*) by the average duration of OC use among ever-users within each age group. We estimated OC prevalence for the years 1965, 1970, 1975, 1980, 1985, 1990, and 1995 using data from seven studies conducted by NCHS between 1965 and 1995: the National Fertility Studies of 1965 and 1970[7,8] and the National Surveys of Family Growth of 1973, 1976, 1982, 1988, and 1995.[9–13] To obtain OC prevalence data in the years 1975, 1980, 1985, and 1990 (the same calendar years as those available for observed rates), we interpolated linearly between prevalence data in the National Survey of Family Growth survey years 1973, 1976, 1982, 1988, and 1995. We assumed that no one used OCs before 1965 or began using them after age 44 years; thus, for women age 45 and above in 1995, OC prevalence data at age 40–44 were used for women of the same cohort in later years. We obtained the average duration of OC use among ever-users, with data provided by Dawson.[14]

To predict 1995 incidence rates based on trends in these risk factors, we fit a model in which changes in these attributes induce proportional changes in incidence rates. We modeled the ovarian cancer incidence rate I_j among women in the jth 5-year age group in 1995 as

$$I_j = I_{0j} \exp(ax_j + by_j)$$

I_{0j} represents the incidence rate in the jth age group in the period 1969–1971, x_j is the difference between the average number of childbirths in 1995 and 1970 for women in age group j, and y_j denotes the change in mean years of OC use from 1970 to 1995 among women in age group j, assuming that the duration in 1970 was zero. The constants a and b, which represent the change in log rate per unit change in parity and in duration of OC use, respectively, were obtained from a combined analysis of 12 U.S. case-control studies of ovarian cancer.[5] These case-control data suggest that the rate ratio associated with parity changes with age. Therefore, we used age-specific values for a that correspond to rate ratios of 0.72 for age 30–39 years, 0.78 for age 40–49 years, 0.80 for age 50–59 years, and 0.86 for age 60–64 years, for the decrease in ovarian cancer risk per childbirth. The value for b corresponds to a rate ratio of 0.90 for the decrease in cancer risk per year of OC use.

We also predicted rates based on changes in parity and changes in OC prevalence (ever-use *vs* never-use). To do so, we assumed $\log(I_j/I_{0j}) = ax_j + cz_j$, where z_j is the difference between OC prevalence in 1995 and 1970 among women in age group j. The constant c corresponds to a rate ratio of 0.66 for cancer risk related to ever-use *vs* never-use of OCs.

Results

Figure 1 shows temporal trends in observed ovarian cancer incidence and mortality rates during the period 1970 through 1995. Rates tend to decline with time among women age 35–59. Mortality rates in particular have declined steadily in all age groups.

Figure 2 shows changes in estimated average parity and duration of OC use among women in 1995, specific for year of birth. Parity reaches a maximum in the cohort of women born in 1931–1935, who averaged more than three childbirths per woman, and declines monotonically thereafter. In contrast, duration of OC use rises continually from a low of <0.5 years among women born in 1921–1925 (who were age 35–39 and therefore had largely completed their reproductive years when OCs were introduced in the early 1960s) to a high of >5 years

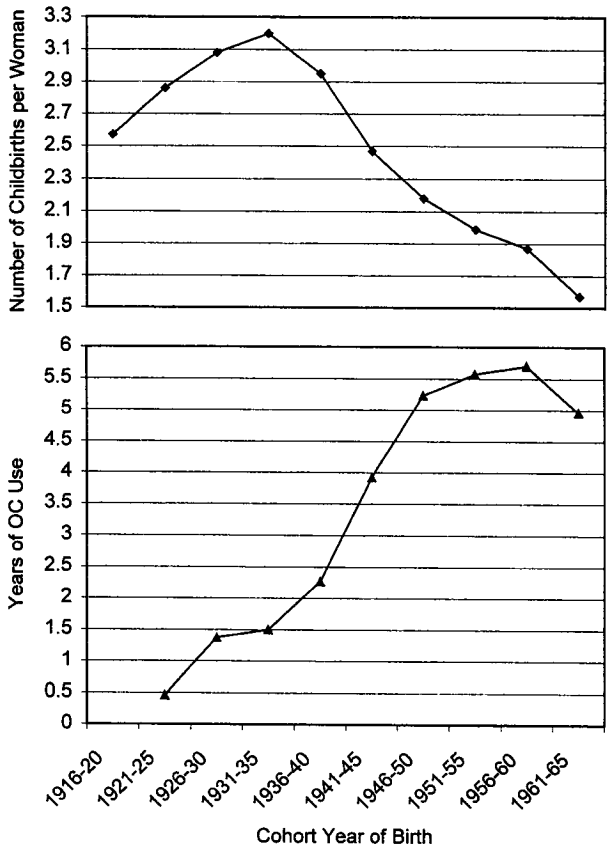

FIGURE 2. Average parity and duration of oral contraceptive use among U.S. women in 1995, by year of birth.

among women born in 1956–1960. Moreover, the duration of use in more recent cohorts will continue to rise, because these women have not completed their reproductive years.

Figure 3 compares the ovarian cancer incidence rates observed in 1970 with those observed in 1995, and with incidence rates predicted for 1995 by temporal changes in parity and duration of OC use, according to the proportional hazards model shown for incidence I_j in the equation. Among premenopausal women (*ie*, those <50 years of age), ovarian cancer rates predicted by the model agree well with the observed declines in incidence. The figure, however, shows discrepancies between observed and predicted rates in 1995 among postmenopausal women age 50–64. For these women, the model predicts stronger declines in incidence rates than were observed. When incidence rates were computed according to changes in OC prevalence (rather than duration of use), the discrepancies noted in Figure 3 persisted.

Discussion

To examine the possibility that the observed declines in ovarian cancer incidence rates in U.S. women 35–59 years of age during 1970–1995 might be explained by changes in parity and OC use, we compared 1995 incidence rates with rates predicted by temporal changes in

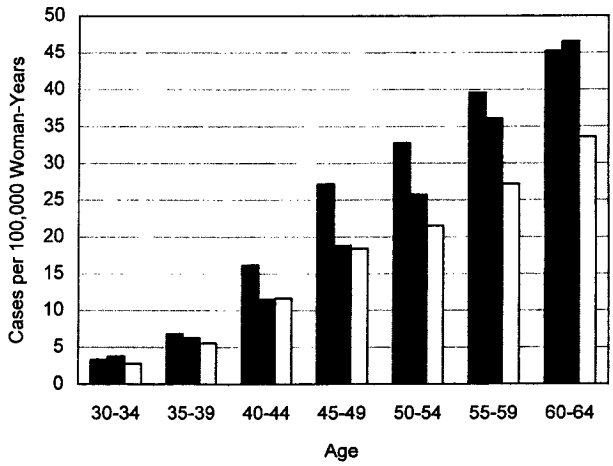

FIGURE 3. Observed and predicted ovarian cancer incidence rates, 1970–1995. ▨ = observed incidence, 1970; ■ = observed incidence, 1995; □ = predicted incidence, 1995.

these characteristics. We found that the observed and predicted rates agreed well among premenopausal women, but that observed rates were substantially higher than predicted rates in postmenopausal women 50–64 years of age. In calculating the predicted rates, we assumed that the risk reduction associated with OC use is proportional to the incidence rate. The data among the postmenopausal women, however, fail to support this assumption, because the 1995 rates in these age groups are substantially larger than predicted. Indeed, the data indicate that the relative decrease in incidence per year of OC use declines with age. Studies of the long-term effects of OC use in postmenopausal women will elucidate this observed decline.

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